

Overview of acute renal manifestations in cancer patients

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Abstract

Acute kidney injury is frequently encountered in patients with malignancy and is associated with prolonged hospitalization, significant morbidity, and increased mortality. Thorough evaluation is required to identify possible contributing factors, which may range from relatively easily reversible pre-renal causes to complex cancer-specific aetiologies. This review will serve as a practical guide for acute care physicians on the acute medical unit to the assessment and initial management of cancer patients presenting with acute kidney injury.

Keywords

acute kidney injury, acute medical unit, malignancy, onco-nephrology

Case

A 67-year-old woman presented to hospital with a 3 day history of frequent episodes of vomiting and diarrhoea. Her past medical history was significant for metastatic renal cell carcinoma diagnosed 6 months previously for which she had undergone radical nephrectomy and radiotherapy. Her post-operative course was complicated by a pulmonary embolism for which she had been on oral anticoagulation with apixaban 5 mg twice daily. She had also been receiving sunitinib (a tyrosine kinase inhibitor) for her metastatic malignancy for about 3 months. She was taking no other regular medication and had no history of exposure to nephrotoxic drugs. On examination, she was pyrexial with a temperature of 38.2 C. Her heart rate was 90/min, blood pressure 110/70 mmHg, oxygen saturation 94% on room air and urine output 20–30 mL/hour. Clinical examination showed evidence of volume depletion but was otherwise unremarkable. Blood results included: haemoglobin 88 g/L (reference range 130–170), white cell count $6.0 \times 10^9/L$ (4–10), neutrophils $4.81 \times 10^9/L$ (2–7), platelets $380 \times 10^9/L$ (150–410), serum creatinine 482 $\mu\text{mol/L}$ (59–104) with a baseline of 96 one week earlier, urea 13.3 mmol/L (1.7–7.1), C-reactive protein 64 mg/L (4–10), potassium 4.5 mmol/L (3.5–5.3), adjusted calcium 2.57 mmol/L (2.2–2.6), albumin 13 g/L (35–50). She was initially treated with intravenous fluid and empirical antibiotic therapy. She also underwent a non-contrast computed tomography scan of the urinary tract; this revealed a mildly enlarged right kidney but no hydronephrosis. Over the next few days, her kidney function continued to deteriorate with a further significant rise in her serum creatinine to 737 $\mu\text{mol/L}$, so she was transferred to the tertiary renal unit for further evaluation and consideration of haemodialysis. At this point, more tests results were available: urine protein to creatinine ratio was 1373 mg/mmol (0–20), but renal immunology

screen including antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), and anti-glomerular basement membrane antibodies (anti-GBM) were normal. A working diagnosis was made of acute kidney injury due to volume depletion and sepsis superimposed on pre-existing proteinuric intrinsic renal disease (perhaps attributable to adverse renal effects of her tyrosine kinase inhibitor) and/or renal cell carcinoma-related glomerulonephritis such as membranous nephropathy or minimal change disease. As her renal function did not improve, she was established on regular haemodialysis. Renal biopsy was considered but not carried out due to the high risk to benefit ratio in the setting of a single functioning kidney.

Introduction

Acute kidney injury (AKI) is a common occurrence in cancer patients, and its incidence has increased in recent decades with advances in the treatment of malignancy and associated improved life expectancy. Multiple factors may contribute, including direct infiltration or mechanical obstruction by tumour, paraneoplastic phenomena (such as glomerulonephritis or tubulointerstitial disease), potentially nephrotoxic chemotherapeutic or intravenous contrast agents, tumour lysis syndrome, thrombotic microangiopathy, hypercalcaemia, complications related to haematopoietic stem cell transplantation, and other general issues (e.g. sepsis, volume depletion). As with all cases of AKI, general measures (such as correction of haemodynamic status, reversal of obstructive uropathy, cessation of nephrotoxic drugs, and close monitoring of fluid balance and biochemistry) can help promote renal recovery and improve patients' outcomes. However, as the aetiology of AKI in patients with malignancy can be more complex and have significant consequences (such as the requirement for renal replacement therapy and / or admission to

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critical care units, or precluding patients from specific therapies for their malignancy or from being enrolled in clinical trials), a more multidisciplinary approach is often required, potentially including acute physicians, nephrologists, haemato-oncologists, and intensive care physicians. It is therefore important for these professionals to have an understanding of the emerging field of onco-nephrology.

Epidemiology and Prognosis

AKI in patients with cancer can have a considerable negative impact on hospital length of stay and cost of treatment, and can result in a significant increase in morbidity and mortality. This was demonstrated in a retrospective observational study by Candrilli and colleagues, in which data were analysed from a United States nationwide inpatient sample pool of patients with haematological malignancies divided into three subgroups: 350,601 patients without AKI, 27,654 patients with AKI not requiring dialysis, and 5148 patients with AKI requiring dialysis. It revealed that the average length of stay and costs among these groups were 7.4, 12.2, and 17.6 days, and \$13,947, \$25,638, and \$44,619 respectively.¹ The incidence of AKI in cancer patients is largely influenced by the type of cancer, stage of disease, and therapy administered. Those who are critically ill, have haematological malignancy undergoing chemotherapy or stem cell transplantation, or who have renal cell carcinoma and undergo radical nephrectomy are at particularly high risk of AKI.² In a Danish study, 37,267 incident cancer patients from a population of 1.2 million were followed up between 1999 and 2006. The 1 year and 5 year risks of AKI were 17.5% and 27% respectively. The incidence of AKI was highest in patients with kidney cancer (44% of patients developed AKI), liver cancer (33%), multiple myeloma (31.8%), and those with distant metastases at the time of cancer diagnosis. About 5% of patients needed to commence renal replacement therapy (RRT) in the form of dialysis within one year of AKI onset.³ AKI requiring RRT is a poor prognostic indicator in patients with cancer, with a 28 day in-hospital mortality rate of around 66–88%.⁴ However, the presence of malignancy should not preclude the patient from initiation of RRT, and a team-based decision is always required. More importantly, an individualised care plan needs to be made between nephrologists and haemato-oncologists after taking into account other significant factors such as age, frailty, performance status, co-morbid conditions, cancer prognosis, and quality of life.

Assessment of kidney function

An accurate assessment of kidney function is paramount in patients with neoplastic disease

in order to allow early recognition and accurate monitoring of acute and chronic kidney injuries. It also facilitates correct dosing of chemotherapeutic agents (minimising the chance of nephrotoxicity) and the addition of preventive measures to minimise further worsening of renal function.^{5–6} Measurement of serum creatinine and use in formulae to estimate creatinine clearance or glomerular filtration rate (GFR), such as the Cockcroft-Gault, Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations, are commonly used in daily clinical practice and can provide reasonable estimates of kidney function. However, given that serum creatinine concentration can be altered by many factors including dietary protein intake, muscle mass, gender, and proximal tubular creatinine secretion, there are certain pitfalls of which clinicians need to be aware in evaluating renal function. For instance, serum creatinine levels can be spuriously low in cancer patients due to cachexia or reduced muscle mass, leading to an overestimation of GFR if estimation is based on creatinine-based formulae such as those listed above. In addition, the pharmacokinetics of anti-cancer agents are poorly understood in patients on acute or chronic haemodialysis, and therefore it is important for oncologists to work closely with nephrologists and renal pharmacists with regard to dose adjustment and timing of administration in order to reduce the risk of systemic and renal toxicities while still delivering an effective dose.⁶

Causes of AKI in cancer patients

AKI can be due to cancer-specific and cancer non-specific causes,⁷ summarised in Table 1.

Table 1. Classification of causes of AKI in cancer patients

Cancer-specific causes	Cancer non-specific causes
Malignant infiltration	Sepsis
Glomerular disease	Volume depletion
Thrombotic microangiopathy	Contrast nephropathy
Tubulointerstitial disease	Non-cancer drugs
Cast nephropathy	
Obstructive uropathy	
Hypercalcaemia	
Tumour lysis syndrome	
Nephrotoxic anti-cancer therapy	
Hepatic sinusoid obstructive syndrome	

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Table 2. Aetiologies of AKI (Acute Kidney Injury)

Pre-renal aetiologies	
Sepsis	
Volume depletion	
Abdominal compartment syndrome	
Non-cancer drugs	
Hypercalcaemia	
Intrinsic aetiologies	
Glomerular	
• Membranous nephropathy	
• Minimal change disease	
• Focal segmental glomerulosclerosis	
• Membranoproliferative glomerulonephritis	
• Amyloidosis	
• Immunoglobulin deposition	
Tubulointerstitial	
• Acute tubular necrosis	
• Lymphomatous infiltration	
• Acute interstitial nephritis	
• Tumour lysis syndrome	
• Cast nephropathy	
Vascular	
• Thrombotic microangiopathy	
Post-renal aetiologies	
Obstruction due to primary or metastatic disease	
Retroperitoneal lymphadenopathy	
Retroperitoneal fibrosis	
Abdominal compartment syndrome	
Stone disease	

To aid in ascertaining the cause of AKI in patients with cancer, aetiologies may be divided into pre-renal, intrinsic and post-renal (Table 2).⁸

Pre-renal aetiologies

Pre-renal AKI frequently occurs in this population. Sepsis is the most common cause of AKI in critically ill patients with cancer, mediated by altered renal blood flow as a result of vasodilation; consequent ischaemia together with cytokine activation lead to acute tubular necrosis.^{7,9–10} Patients with cancer often develop volume depletion due to diarrhoea and vomiting following chemotherapy.^{7–10} Mucositis and oesophagitis due to radiotherapy or chemotherapy (e.g. with methotrexate or capecitabine) can lead to reduced oral intake and severe volume depletion, particularly in those with head and neck cancer.¹¹

Malignant ascites can give rise to an intra-abdominal compartment syndrome, potentially causing dysfunction of multiple organ systems such as the kidneys, heart, lungs, and gut. This is mainly mediated by compromise of arterial and venous flow but can also lead to obstructive uropathy.

The diagnosis is usually made based on clinical suspicion, high intra-abdominal pressure (above 20mmHg), and rapid improvement after abdominal decompression.¹²

Common medications such as diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or nonsteroidal anti-inflammatory agents can also contribute to pre-renal AKI due to altered intrarenal haemodynamics. Hypercalcaemia is present in 20–30% of cancer patients and can lead to AKI as a result of renal vasoconstriction and volume depletion from natriuresis and diuresis.¹³

Intrinsic aetiologies

Glomerular disease

Haematological malignancies such as myeloma can lead to the deposition of immunoglobulin components (including amyloid) within glomeruli. In addition, “paraneoplastic” glomerulonephritis may occur, where the mechanism is unclear but is thought to involve circulating products from cancer cells. Most patterns of glomerulonephritis have been described in cancer patients, but membranous nephropathy is the most frequent glomerular pathology in those with solid tumours, whereas minimal change disease is the commonest in haematological malignancies.¹⁴ Patients often present with nephrotic syndrome, and treatment is of the underlying malignancy.

Thrombotic microangiopathy (TMA)

Most cases in cancer patients are associated with disseminated malignancy, particularly gastric, breast and colorectal cancer, or with anti-cancer drugs.¹⁵ It may occur in the context of disseminated intravascular coagulation (due to the malignancy itself or as a result of sepsis or anti-cancer drugs) or thrombotic thrombocytopenic purpura. The pathogenesis is not well understood. The mainstay of therapy is treatment of the underlying malignancy. Cancer-associated TMA does not generally respond well to plasma exchange.⁸

Lymphomatous infiltration

A fairly common but under-appreciated complication of haematological malignancies, as it is often subclinical.¹⁶ It is thought that pressure elevation within the intraglomerular and interstitial compartments plays a mechanistic role in AKI.¹⁷ Diagnosis is made by renal biopsy, and chemotherapy often results in significant improvement in renal function.

Tumour lysis syndrome (TLS)

This is most common in haematological malignancies with a large tumour burden. It can

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occur spontaneously due to high cell turnover or, more commonly, as a result of cell death following chemotherapy. The widespread necrosis of tumour cells causes release of intracellular contents (particularly purines, potassium, and phosphate) into the circulation. This can cause an array of electrolyte disturbances (hyperuricaemia, hyperkalaemia, hyperphosphataemia, hypocalcaemia) and AKI due to deposition of products of purine breakdown including uric acid or xanthine.¹⁸ Other organs may also be affected including the brain (potentially causing seizures) and the heart (leading to arrhythmias). Risk stratification systems and guidelines for the prevention of TLS exist. In low risk patients the mainstay is maintenance of hydration (orally or intravenously) with or without the use of allopurinol (which prevents de novo uric acid generation by inhibition of xanthine oxidase). Routine use of allopurinol is recommended for medium risk patients. For high risk patients, administration of rasburicase is advocated as this breaks down existing as well as de novo uric acid, but also, unlike allopurinol, does not lead to a potentially harmful increase in xanthine levels.^{9–10,18–19} Treatment of established TLS may include intravenous fluids, correction of electrolyte disturbances, allopurinol, rasburicase, and dialysis if indicated.

Cast nephropathy

This is the commonest cause of AKI in patients with myeloma.²⁰ Excess free light chains produced by neoplastic plasma cells overwhelm the reabsorption capacity of the proximal tubular cells, leading them to bind to uromodulin (Tamm-Horsfall protein) in the distal tubule causing obstruction and subsequent AKI.¹⁰ Myeloma can also cause AKI through hypercalcaemia, amyloidosis, cryoglobulinaemia, light or heavy chain deposition disease, and Fanconi syndrome. Treatment with chemotherapy (with the proteasome inhibitor bortezomib being the mainstay of therapy) should be initiated early to reduce free light chain production and maximise the chance of renal recovery.²¹ The removal of free light chains using plasma exchange or haemodialysis with large-pore dialysers remains of unproven benefit and is currently not routinely recommended.²²

Contrast nephropathy

Cancer patients are susceptible to developing contrast nephropathy. They may have multiple risk factors including need for imaging with contrast, pre-existing chronic kidney disease, volume depletion, and use of other nephrotoxic agents. Intravenous iodinated contrast agents cause AKI through renal vasoconstriction and direct tubular toxicity; this usually occurs 48–72 hours after

contrast administration.²³ Pre- and post-contrast intravenous fluid therapy (0.9% saline or 1.26% sodium bicarbonate) can help minimise the risk.²³ The role of N-acetylcysteine (NAC) in prevention of contrast-induced nephropathy remains controversial in practice. In one meta-analysis of randomised controlled trials, it was concluded that oral NAC supplementation was associated with a significant reduction in serum creatinine level and risk of contrast nephropathy.²⁴ This potential benefit of oral NAC was further examined in the most recent PRESERVE trial in which no considerable differences in clinical outcomes being observed comparing oral NAC with placebo for patients undergoing angiography.²⁵

Haematopoietic stem cell transplantation (HSCT)

AKI is a frequent complication of HSCT, and is more common after myeloablative compared to non-myeloablative regimens.^{7–10,26–27} Sepsis and the use of nephrotoxic antimicrobials (such as amphotericin B) and calcineurin inhibitors are common precipitants of AKI.^{9–10} However, other factors can also contribute such as TLS, TMA, and hepatic sinusoidal obstruction syndrome (discussed below). Graft versus host disease also increases the risk of AKI, where renal injury can include glomerular disease (such as membranous nephropathy) and tubulitis.²⁷

Hepatic sinusoidal obstruction syndrome

Previously known as hepatic veno-occlusive disease, this usually occurs a few weeks after initiation of conditioning regimens with cytotoxic agents for HSCT or other malignancies. Patients typically present with abdominal pain, jaundice, ascites, hepatomegaly, and other features of portal hypertension. The likely mechanism is injury to the hepatic sinusoidal endothelium resulting in sinusoidal thrombosis and obstruction, with subsequent liver and kidney failure. Most patients recover with supportive therapy. In severe cases, the use of defibrotide (a polydisperse oligonucleotide with local antithrombotic and pro-fibrinolytic properties) has shown benefit in some studies.^{7,9–10,27}

Thromboembolism / vascular invasion

Patient with cancer are at increased risk of renal vein thrombosis due to the hypercoagulable state often associated with malignancy; this risk is particularly high in patients with nephrotic syndrome, either related to the cancer itself or to some chemotherapeutic agents (listed in table 2). Arterial thrombosis is less common. Direct tumour invasion into vessels can also occur, particularly in renal and hepatocellular carcinomas.^{7–10,28}

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Table 3. Summarising the renal effects of anti-cancer medication

Anti-cancer agent	Renal disease
Cisplatin	AKI due to vasoconstriction, cytokine release, tubular cell injury Tubular toxicity causing electrolyte disturbance (e.g. ↓Mg) Thrombotic microangiopathy
Methotrexate	AKI due to tubular obstruction from precipitation of methotrexate and insoluble metabolite (7-hydroxymethotrexate)
Gemcitabine	Thrombotic microangiopathy
Ifosfamide	AKI due to tubular cell injury Fanconi syndrome Nephrogenic diabetes insipidus
Interferon-α	Minimal change disease Focal segmental glomerulosclerosis
Tyrosine kinase inhibitors (sunitinib, sorafenib, axitinib, cediranib)	Hypertension and proteinuria Thrombotic microangiopathy Interstitial nephritis
Immune checkpoint inhibitors (anti-cytotoxic T-lymphocyte-associated protein 4, anti-programmed death antibodies)	Interstitial nephritis Membranous nephropathy Minimal change disease Thrombotic microangiopathy

Nephrotoxic anti-cancer therapy

There are multiple anti-cancer therapies that can cause renal disease (Table 3). Toxic renal effects include glomerular disease, tubular injury / dysfunction, interstitial nephritis, TMA and crystal nephropathy. AKI is the most frequent mode of presentation, but others (such as electrolyte disturbances or proteinuria) may also occur.

It is vital for any treating clinician to be aware of the risk of deleterious renal effects of co-prescribing certain medications for cancer patients. For example, gentamicin should be avoided within 7 days of cisplatin therapy due to the risk of nephrotoxicity and ototoxicity.^{7–10, 17,23} Vancomycin can also lead to tubular cell injury. Macrolide antibiotics such as clarithromycin (which is commonly used to treat pneumonia) and antifungal agents such as fluconazole should be avoided in patients taking tacrolimus (sometimes used for treatment of immunotherapy-related hepatitis or nephritis) as inhibition of the cytochrome P450 system leads to a rise in tacrolimus levels, increasing the potential for nephrotoxicity.^{7–10} Penicillins, ciprofloxacin, and proton pump inhibitors can cause a tubulointerstitial nephritis.^{17,23} Statins may lead to an increased risk of rhabdomyolysis, particularly when used concurrently with medications that inhibit the cytochrome P450 system.^{17,23}

Post-renal aetiologies

Urinary tract obstruction should always be considered when cancer patients have AKI. Post-renal AKI is often due to bladder outlet obstruction or ureteric obstruction (either intrinsic or extrinsic). Solid organ

tumours that most commonly cause obstruction include bladder, prostate, uterine and cervical malignancies.²⁹ Ureteric obstruction can also result from retroperitoneal lymphadenopathy. Radiotherapy to the abdomen and pelvis can cause retroperitoneal fibrosis, which can also lead to extrinsic urinary tract obstruction.^{29–30} Early relief of obstruction with nephrostomies or ureteric stents can improve renal function, but prognosis is dictated by the underlying malignancy and is often poor.³⁰ As discussed above, abdominal compartment syndrome due to malignant ascites may also result in obstructive uropathy.

Evaluation and management of AKI in Cancer Patients

The same general principles for assessing and managing AKI in any patient also apply to cancer patients. History and examination, in particular evaluation of fluid balance and identification of nephrotoxic medications, are the cornerstones of assessment. This section will highlight the key aspects of management of AKI in cancer patients. After the initial assessment on the acute medical unit, the oncology and nephrology teams should be involved in the care of these patients.

Initial assessment

History

Key points to elicit

- Preceding illness such as gastroenteritis, or lower respiratory tract or urinary tract infection
- Pre-existing renal disease

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- Co-morbidities increasing risk of AKI including diabetes, hypertension, cardiovascular disease
- Cancer diagnosis and prognosis
- Anti-cancer therapy and duration
- Nephrotoxic medication such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics, other anti-hypertensive agents, non-steroidal anti-inflammatory drugs, proton pump inhibitors, antibiotics, herbal remedies

Examination

- Basic observations: blood pressure, heart rate, temperature, respiratory rate, oxygen saturations
- Cardiovascular, respiratory, and abdominal examinations

Fluid balance

- Skin turgor
- Oedema
- Capillary refill
- Jugular venous pressure
- Pulse rate
- Lying and standing blood pressure
- Urine output
- Chest radiograph

Intravenous fluids should be initiated after the examination if there is evidence of dehydration or hypovolaemia. If the patient is fluid overloaded, intravenous furosemide may be tried. Antibiotics should be started promptly if there is any suspicion of infection. All nephrotoxic agents should be suspended. Urine output should be monitored closely. Urinary catheterisation should be avoided if possible due to the risk of infection, but may be necessary if the patient is unable to cooperate or if there is evidence of bladder outflow obstruction.

Further assessment

Urinalysis

- Blood and / or protein on dipstick – consider glomerular or tubular disease
- Urine protein: creatinine ratio should be tested to quantify proteinuria if protein present on dipstick
- Nitrites and leucocytes on dipstick – consider infection
- Urine culture should be sent if possibility of urine infection
- Glycosuria (in the absence of diabetes) may indicate Fanconi syndrome

- Urine microscopy may show red cell casts (indicative of glomerulonephritis) or crystals (e.g. urate in TLS)

Blood tests

- Obtain previous baseline creatinine if available and recent trend – determines stage of AKI
- Inflammatory markers – raised white cell count and / or C-reactive protein can indicate infection or other inflammatory process
- Albumin – low albumin can suggest nephrotic syndrome, but may also be present in cachectic / malnourished / catabolic cancer patients
- Electrolytes: potassium, sodium, phosphate, magnesium, calcium, bicarbonate – pattern of electrolyte disturbance may be suggestive of tubular injury or TLS, and may require urgent treatment
- Uric acid – raised in TLS
- Haemoglobin, platelets, bilirubin, lactate dehydrogenase, haptoglobin – anaemia, thrombocytopenia, increased lactate dehydrogenase and bilirubin, low haptoglobin and negative Coombs test suggest TMA
- Blood film – schistocytes are present in TMA
- Coagulation screen – abnormal in disseminated intravascular coagulation
- Myeloma screen: serum paraprotein, serum free light chains, immunoglobulins
- ADAMTS-13 (“a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13”) – if thrombotic thrombocytopenic purpura is suspected
- Microbiological testing (e.g. blood cultures, viral studies) where appropriate

Blood results will help determine the severity of AKI and assist with establishing the underlying diagnosis. Electrolyte disturbances should be corrected. If the patient requires dialysis the nephrology team should be contacted urgently. Standard indications for initiation of acute dialysis (refractory hyperkalaemia, pulmonary oedema, metabolic acidosis, and uraemic encephalopathy/pericarditis) would be applied, but individualised decisions should be made by nephrologists based on the patient's wishes, clinical condition and prognosis.

Chest radiograph

- May show evidence of pulmonary oedema, infection, malignant involvement of lungs, mediastinal lymph nodes, or bones

Ultrasound

- Urgent imaging is indicated if obstructive uropathy is suspected – this should be

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performed within 24 hours, or within 6 hours if pyonephrosis is suspected

- Bladder distension is suggestive of bladder outflow obstruction and requires urgent catheter insertion
- Hydronephrosis not due to bladder outflow obstruction warrants urgent urology / interventional radiology involvement with a view to nephrostomy or retrograde ureteric stent insertion to relieve obstruction if appropriate

Renal biopsy

- If the cause of AKI is unclear, or if glomerular or tubulointerstitial nephritis is suspected, a renal biopsy may be needed to confirm the diagnosis and assist with prognosis

Renal replacement therapy in cancer patients with AKI

Dialysis is normally offered to patients with potentially curable cancer. However, in those with a guarded prognosis the decision is more challenging. A frank discussion about what dialysis entails (together with the potential risks, benefits and possible outcomes) is required. There should be shared decision making with involvement of the patient, family, and nephrology, oncology, and palliative care teams.³¹ Although the patient may be nearing the end stage of their life, dialysis may still be appropriate in order to give them more time with their family. However, if they are very frail or have advanced disease or multiple other comorbidities, dialysis can significantly reduce their quality of life and may reduce or have no effect on their length of life. Where dialysis is instituted, the patient should be reviewed regularly to assess their clinical condition and agree whether ongoing dialysis is in their best interests.

Conclusion

AKI occurs commonly in patients with malignancy. It is often multifactorial, and a structured approach with a comprehensive clinical assessment is warranted, in particular to identify cancer-specific contributory factors. Early recognition and effective management of the underlying causes not only reduce irreversible kidney damage, but also minimise interruption of anti-cancer therapy and consequent effects on underlying disease progression. Abnormal renal function has been established as a poor prognostic factor in cancer patients and has also been shown to be associated with significant additional morbidity and mortality. Advances in the field of oncology in the last few decades have led to the development of less toxic treatments with greater efficacy. Although this has resulted in improved survival of cancer patients and the ability to treat patients who would previously have been regarded as too unwell or frail, it has posed the additional challenge of increasing the incidence of disease or therapy-related complications in a patient population that is becoming older and has more comorbidities. Therefore, novel pathways and models of care should be developed in order to mitigate the risk and improve the management of AKI in cancer patients. This requires an increased awareness of these issues by oncologists, physicians, and nephrologists and liaison between these groups. Furthermore, the development of nephrologists with a special interest in onconeurology will lead to an increased understanding of the increasingly complex patterns of acquired renal diseases associated with malignancy and anti-cancer therapies.

Conflict of interest

Nothing to declare.

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References

- Candrilli S, Bell T, Irish W, *et al.* A comparison of inpatient length of stay and costs among patients with hematologic malignancies (excluding Hodgkin disease) associated with and without acute renal failure. *Clin Lymphoma Myeloma*. 2008; **8**: 44–51.
- Darmon M, Cirotti M, Thiery G, *et al.* Clinical review: specific aspects of acute renal failure in cancer patients. *Crit Care*. 2006; **10**(2):211.
- Christiansen CF, Johansen MB, Langeberg WJ, *et al.* Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. *Eur J Intern Med*. 2011; **22**(4):399–406.
- Benoit DD, Hoste EA. Acute kidney injury in critically ill patients with cancer. *Crit Care Clin*. 2009; **26**: 151–179.
- Launay-Vacher V, Janus N, Deray G. Renal insufficiency and cancer treatments. *ESMO Open*. 2016; **1**(4):e000091.
- Aapro M, Launay-Vacher V. Importance of monitoring renal function in patients with cancer. *Cancer Treat Rev*. 2012; **38**(3):235–40.
- Cohen E, Krzesinski J-M, Launay-Vacher V, *et al.* Onco-Nephrology: Core Curriculum 2015. *Am J Kidney Dis* 2015; **66**(5): 869–883.
- Kitai Y, Matsubara T, Yanagita M. Onco-nephrology: current concepts and future perspectives. *Japanese Journal of Clinical Oncology*. 2015; **45**(7):617–628.
- Lahoti A, Humphreys BD. Chapter 3: AKI Associated with Malignancies. Onco-Nephrology Curriculum. *American Society of Nephrology* 2016.
- Lam AQ, Humphreys BD. Onco-Nephrology: AKI in the Cancer Patient. *Clin J Am Soc Nephrol* 2012; **7**: 1692–1700.
- Campos MI, Campos CN, Aarestrup FM, *et al.* Oral mucositis in cancer treatment: Natural history, prevention and treatment. *Mol Clin Oncol*. 2014; **2**(3):337–340.
- Bailey J, Shapiro MJ. Abdominal compartment syndrome. *Crit Care*. 2000; **4**(1):23–9.
- Stewart AF. Clinical Practice. Hypercalcaemia associated with cancer. *N Engl J Med*. 2005; **352**: 373–379.
- Jhaveri KD, Shah HH, Patel C, *et al.* Glomerular diseases associated with cancer, chemotherapy, and hematopoietic stem cell transplantation. *Adv Chronic Kidney Disease* 2014; **21**:48–55.
- Lesesne JB, Rothschild N, Erickson B, *et al.* Cancer-associated haemolytic-uremic syndrome: analysis of 85 cases from a national registry. *J Clin Oncol* 1989; **7**:781–9.
- Cohen LJ, Rennke HG, Laubach JP, *et al.* The spectrum of kidney involvement in lymphoma: A case report and review of the literature. *Am J Kidney Dis*. 2010; **56**: 1191–1196.
- Nephrology Secrets, 4th edition. Lerma, Sparks and Topf, 2018.
- Abu-Alfa AK, Younes A. Tumor lysis syndrome and acute kidney injury: evaluation, prevention, and management. *Am J Kidney Dis*. 2010; **55**(5 Suppl 3):S1–13; quiz S14–9.
- G. L. Jones, A. Will, G. H. Jackson, *et al.* The British Committee for Standards in Haematology, “Guidelines for the management of tumour lysis syndrome in adults and children with haematological malignancies on behalf of the British Committee for Standards in Haematology,” *British Journal of Haematology*, vol. **169**, no. **5**, pp. 661–671, 2015.
- Montseny JJ, Kleinknecht D, Meyrier A, *et al.* Long-term outcome according to renal histological lesions in 118 patients with monoclonal gammopathies. *Nephrol Dial Transplant*. 1998; **13**: 1438–1445.
- Hutchison CA, Cockwell P, Stringer S, *et al.* Early reduction of serum-free light chains associates with renal recovery in myeloma kidney. *J Am Soc Nephrol* 2011; **22**: 1129–36.
- Myeloma: diagnosis and management. *NICE guidelines*, 2016.
- The Oxford Handbook of Nephrology and Hypertension, 2nd edition. Steddon and Ashman 2014.
- Xu R, Tao A, Bai Y, Deng Y, *et al.* Effectiveness of N-Acetylcysteine for the Prevention of Contrast-Induced Nephropathy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Am Heart Assoc*. 2016; **5**(9).
- Weisbord SD, Gallagher M, Jneid H, *et al.* Outcomes after angiography with sodium bicarbonate and acetylcysteine. *N Engl J Med*. 2018; **378**: 603–14.
- Zager RA. Acute renal failure in the setting of bone marrow transplantation. *Kidney Int* 1994; **46**: 1443–1458.
- Lopes JA, Jorge S. Acute kidney injury following HCT: Incidence, risk factors and outcome. *Bone Marrow Transplant*. 2011; **46**: 1399–1408.
- Quencer KB, Friedman T, Sheth R, *et al.* Tumor thrombus: incidence, imaging, prognosis and treatment. *Cardiovasc Diagn Ther*. 2017; **7**(Suppl 3):S165–S177.
- Humphreys BD, Soiffer RJ, Magee CC. Renal failure associated with cancer and its treatment: an update. *J Am Soc Nephrol*. 2005; **16**: 151–61.
- Vaglio A, F. Maritati. Idiopathic Retroperitoneal Fibrosis. *J Am Soc Nephrol*. 2016; **27**(7): p. 1880–9.
- Scherer JS, Swidler MA. Decision-making in patients with cancer and kidney disease. *Adv Chronic Kidney Dis*. 2014; **21**(1):72–80.